

Medication adherence in HIV-positive pregnant women on antiretroviral therapy attending antenatal clinics in Ado metropolis, south-west Nigeria: A multicentre study

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Background. Adherence to antiretroviral therapy (ART) and optimal viral suppression are crucial to the prevention of mother-to-child transmission (PMTCT) of HIV/AIDS.

Objective. To determine adherence to ART and associated factors in Ado-Ekiti, Nigeria.

Methods. A cross-sectional multicentre study was conducted among 170 HIV-positive pregnant women attending antenatal clinics of Ekiti State University Teaching Hospital and the Comprehensive Health Centre in Ado-Ekiti. Data collected using a semi-structured questionnaire were analysed with SPSS. Descriptive statistics, univariate and logistic regression were performed to determine factors associated with good adherence.

Results. Using the pill count method and the Morisky Medication Adherence Scale-8 (MMAS-8), the prevalence of good adherence was 73.5% and 75.3%, respectively. Women with higher education were three times more likely to practise good adherence than those with little or no formal education (adjusted odds ratio (aOR)=3.03; 95% confidence interval (CI) 1.23 - 5.79; $p=0.043$) and those employed were four times more likely to practise good adherence (aOR=4.13; 95% CI 1.83 - 8.15; $p=0.02$). Also, partner disclosure, treatment support and use of ARVs for prevention of mother-to-child transmission (PMTCT) were indications of women three times more likely to practise good adherence ((aOR=2.53; 95% CI 0.99 - 5.80; $p=0.035$); (aOR=2.15; 95% CI 0.77 - 4.15; $p=0.014$) and (aOR=3.15; 95% CI 0.93 - 6.21; $p=0.035$)). Forgetfulness, busy schedule and stigmatisation were reasons given for non-adherence.

Conclusions. The majority of the women had good adherence. However, counselling on adherence and partner disclosure should be sustained to ensure full benefits of PMTCT.

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Prevention of mother-to-child transmission (PMTCT) is a pillar in the elimination of vertical transmission of HIV, with considerable efforts made towards appropriate interventions.^[1] In 2017, ~180 000 children were newly infected with HIV, with 88% in sub-Saharan Africa and the majority of whom infected through mother-to-child transmission (MTCT).^[2] Nigeria has the highest rate of MTCT of HIV globally, despite the low prevalence of HIV, with 37 000 children newly infected with HIV in 2017.^[3] The risk of MTCT ranges between 25% and 48% without any intervention, while this risk is reduced to <2% and 5% with appropriate interventions in non-breastfeeding and breastfeeding mothers, respectively. Most MTCT occurs in the intrapartum period.^[4,5]

The goal of highly active antiretroviral therapy (HAART) in PMTCT is to achieve maximal viral suppression so as to reduce vertical transmission and to provide prophylaxis for the baby.^[6] Successful and positive impact of antiretroviral therapy (ART) requires high rates of adherence. There is a clear relationship between adherence to antiretroviral (ARV) drug treatment, viral load suppression, acquired drug resistance and treatment failure.^[6] Adequate adherence to the prescribed ARV medications is essential to achieving maximal viral suppression necessary to prevent MTCT. Adherence rates exceeding 95% are necessary, in order to maximise

the benefits of ART. Higher levels of drug adherence are associated with improved virological, immunological and clinical outcome.^[7]

Adherence to HAART is complex, requiring patients to remember multiple medications and dosing schedules. Patient failure to follow the ART regimen can lead to the development of treatment-resistant strains and poorer health outcomes.^[8,9] Several studies done in Nigeria have examined adherence to ART among HIV-positive patients,^[10-12] with very few among HIV-positive pregnant women.^[6,13] Studies on adherence to ART among HIV-positive pregnant patients by Igwegbe *et al.*^[6] in south-eastern Nigeria and Ekama *et al.*^[13] in south-western Nigeria reported prevalence rates of 80.6% and 78.3%, respectively. Fear of stigmatisation, discrimination, forgetfulness, feeling of good health, living far away from the hospital and lack of access to transportation, pill burden and side-effects of the drugs were some of the factors found to be associated with suboptimal adherence.^[6,13-15]

There has been no study in Ekiti State on adherence to ARV medication among HIV-positive pregnant women. Therefore, this study was conducted to determine adherence to ART and the associated factors among HIV-positive pregnant women attending antenatal clinics in Ado-Ekiti, south-western Nigeria. Findings from this study will help to influence policy that will strengthen PMTCT services in Ekiti State.

Methods

This was a multicentre cross-sectional study conducted among HIV-positive pregnant women attending antenatal clinics in Ekiti State University Teaching Hospital (EKSUTH) and the Comprehensive Health Centre (CHC), both located in Ado-Ekiti, south-western Nigeria between 1 February 2018 and 31 January 2020. Ado-Ekiti is the capital of Ekiti State with a land area of 293 km² and a population of 308 621 according to the 2006 population census. The majority of inhabitants are Christians and are civil servants, farmers and artisans.

EKSUTH and CHC offer free comprehensive HIV/AIDS services, including PMTCT services. These services are under the sponsorship of the US President's Emergency Plan for AIDS Relief (PEPFAR) through AIDS Prevention in Nigeria (APIN), a non-governmental organisation and Ekiti State Agency for Control of AIDS. Following status determination, every HIV-positive pregnant woman is started on lifelong ART with a single fixed-dose combination tablet of efavirenz, emcitritabine and tenofovir disoproxil fumarate (Atripla), regardless of their clinical status or CD4 count. HIV-positive pregnant women will have at least one CD4 count and viral load estimate done before delivery of their baby to determine whether the HIV-exposed infant is at high risk and eligible for enhanced ART prophylaxis.^[16] Prior to ART commencement, HIV-positive pregnant women receive adherence counselling, provided by nurses and midwives in the antenatal clinic, and ongoing adherence counselling is provided at every refill visit by trained adherence counsellors.

The sample size was calculated using the formula for single proportion. Using the prevalence of 10.8% among pregnant women from a previous study in Nigeria,^[14] a 95% confidence interval (CI), 5% margin of error and 10% contingency for non-respondents, a sample size of 164 was calculated.

All HIV-positive pregnant women with known gestational age attending an antenatal clinic in the study centres, who had been on ARV drugs for at least 3 months prior to the study and gave consent to participate in the study, were included. Those who had not been on ART for up to 3 months and who withheld consent were excluded. The eligible women at both health facilities were counselled about the study by trained research assistants, and those who expressed their willingness to participate were recruited consecutively after signing the informed consent.

Data were collected from the women using a pretested interviewer-administered questionnaire divided into two parts. The first part enquired about sociodemographic characteristics, such as age, parity, educational and occupational status (of the women and their spouses), religion, marital status and socioeconomic status (assessed by adding scores of the women's education level and their husbands' occupation; social classes I and II were categorised as high class, class III as middle class and classes IV and V as low class as described by Olusanya *et al.*^[17]). The second part assessed knowledge of HIV, stigmatisation, partner disclosure, adherence to ARV drugs, use of isoniazid preventive therapy (IPT) and factors that encouraged adherence or non-adherence. Their CD4 count and viral load were extracted from their case records.

Adherence to ARV medication was assessed using the pill count method and the modified Morisky Medication Adherence Scale-8 (MMAS-8). Adherence using the pill count method was ascertained by counting the number of remaining pills in relation to the total number of prescribed doses during the last visit. Adherence status

was termed 'good' when study participants had taken at least 95% of the total drugs at the prescribed dosing interval, while 'poor' adherence status was determined by missing at least 5% of all the doses over the period of a month. The MMAS-8 is an 8-item validated self-reported questionnaire used in assessing adherence of patients to medication.^[18] It examines the knowledge and motivation levels of patients in respect of adherence to their medication. The first seven items on the scale have a binary response (Yes=1, No=0) indicating adherent or non-adherent while the eighth item is answered using a 5-point Likert scale – never; almost never; sometimes; often and always – expressing how often a patient misses taking medication. Adherence level using MMAS-8 was graded in this study as high adherence with a score of 0, medium adherence with a score of 1 and 2, and poor adherence with a score above 2.

The data collected were analysed using the Statistical Package for Social Sciences (SPSS) software, version 22 (IBM Corp., USA). Categorical variables were presented in frequency and percentages while continuous variables were expressed in mean and standard deviation (SD). The χ^2 test was used to test for significance for categorical variables and Student's *t*-test and one-way analysis of variance (ANOVA) for continuous variables. Logistic regression analysis was done to determine factors associated with good adherence among the women, using odds ratios and 95% CIs. A *p*-value <0.05 was considered statistically significant.

The study was approved by the Ethics and Research Committee of Ekiti State Primary Health Care Development Agency and Ekiti State University Teaching Hospital. The women were adequately informed about the study and written informed consent was obtained from them. The data collected were made anonymous and they were at liberty to withdraw from further participation without affecting their care.

Results

A total of 170 HIV-positive pregnant women participated in the study. The study showed that 125 (73.5%) women had good adherence (taking at least 95% of the total drugs at the prescribed dosing interval) using the pill count method while 128 (75.3%) women had a score 2 and below using the MMAS-8. The overall percentage agreement between pill count and self-reported adherence using MMAS-8 was 99.6% with a kappa statistics of 0.99 (*p*<0.001).

The mean (SD) age of the women was 29.82 (5.87) years, mean (SD) gestational age was 29.08 (4.08) weeks, mean (SD) duration of ART use was 3.30 (1.56) years and the median parity and interquartile range were 2, respectively. The majority of women were married (75.9%), had at least primary education (75.3%), were gainfully employed (82.9%) and dwelt in the urban area. Other sociodemographic characteristics of the women are shown in Table 1.

About three-fifths of the women had disclosed their status to their partners (58.8%), displayed good knowledge about HIV (61.8%), had treatment support (58.2%) and had CD4 counts of 350 - 450 cells/mm³ (61.8%). More than two-thirds of the women agreed that ART can prevent MTCT of HIV (67.1%) and had suppressed viral loads (70.0%). Less than half of the women had had PMTCT exposure before (45.9%) and had experienced stigmatisation as a result of their status (47.6%) (Table 2).

Table 3 shows that on univariate analysis, the parity (*p*=0.026), marital status (*p*=0.001), education (*p*=0.005), occupation (*p*=0.001), place of residence (*p*=0.001) and the mean CD4 counts (*p*=0.001)

Table 1. Sociodemographic characteristics of the women in the study (N=170)

Variable	n (%)*
Age (years), mean (SD)	29.82 (5.87)
Parity, mean (SD)	1.77 (1.03)
Gestational age (weeks), mean (SD)	29.08 (4.08)
Duration of ART use (years), mean (SD)	3.30 (1.56)
Marital status	
Married	129 (75.9)
Single	22 (12.9)
Widowed	10 (5.9)
Divorced	9 (5.3)
Education	
None	42 (24.7)
Primary	40 (23.5)
Secondary	38 (22.4)
Tertiary	50 (29.4)
Occupation	
Unemployed	29 (17.1)
Self-employed	32 (18.8)
Privately employed	31 (18.2)
Government employed	78 (45.9)
Religion	
Christianity	107 (62.9)
Islam	63 (37.1)
Place of residence	
Rural	56 (32.9)
Urban	114 (67.1)
Social class	
Low	75 (44.1)
Middle	43 (25.3)
High	32 (30.6)

*Unless otherwise specified.

of the women were significantly associated with good adherence to medication while the age, religion, ethnicity and social class of the women were not significantly associated ($p>0.05$). Also, there was no significant difference in the mean age, parity, gestational age and duration of ARV drugs use among the women with good or poor medication adherence ($p>0.05$).

The univariate analysis of the clinical factors affecting adherence showed that knowledge of HIV ($p=0.001$), status disclosure to partners ($p=0.022$), previous PMTCT ($p=0.049$), use of ART for PMTCT ($p=0.001$), treatment support by partners ($p=0.001$) and low risk of stigmatisation ($p=0.001$) were significantly associated with good medication adherence while duration of ART use was not significantly associated with good adherence, $p>0.05$ (Table 4).

Table 5 shows that post-primary education ($p=0.043$), being employed ($p=0.020$), disclosure of status to partners ($p=0.035$), use of ART for PMTCT ($p=0.035$) and treatment support by partner and relatives ($p=0.014$) were significant determinants of good adherence on regression analysis of the significant variables from univariate analysis.

Discussion

The use of ARV drugs has been established as one of the effective strategies in the reduction of MTCT of HIV infection.^[13] It has been shown that zero MTCT of HIV is achievable when the viral load is undetectable, and this can only be achieved with optimal

Table 2. Clinical characteristics of the women in the study

Variable	n (%)
Adherence status (pill count)	
No	45 (26.5)
Yes	125 (73.5)
Adherence level	
Low	42 (24.7)
Moderate	51 (30.0)
High	77 (45.3)
Partner disclosure	
No	70 (41.2)
Yes	100 (58.8)
Previous PMTCT	
No	92 (54.1)
Yes	78 (45.9)
Knowledge of HIV	
Poor	65 (38.2)
Good	105 (61.8)
Stigmatisation	
No	89 (52.4)
Yes	81 (47.6)
IPT use	
No	13 (7.6)
Yes	157 (92.4)
Treatment support	
No	71 (41.8)
Yes	99 (58.2)
PMTCT	
Yes	56 (32.9)
No	114 (67.1)
Viral loads	
Unsuppressed	51 (30.0)
Suppressed	119 (70.0)
CD4 counts (cell/mm ³)	
<350	31 (18.2)
350 – 450	105 (61.8)
>450	34 (20.0)
Reasons for adherence to drugs (n=125)*	
To protect my unborn child	125 (100.0)
To stay alive and live healthy	111 (88.8)
Previous PMTCT experience	69 (55.2)
Reasons for non-adherence to drugs (n=45)*	
Feeling better	41 (91.1)
Forgetfulness	33 (73.3)
Busy work schedule	31 (68.9)
Side-effects of the drugs	27 (60.0)
Fear of stigmatisation	25 (55.6)

PMTCT = prevention of mother-to-child transmission; MTCT = mother-to-child transmission; IPT = isoniazid preventive therapy.
*Multiple responses.

adherence to ARV drugs. Hence, ART adherence of at least 95% of the drugs taken at prescribed dosing intervals optimises outcome and minimises occurrence of viral resistance.^[19] The adherence prevalence rate found among the HIV-positive pregnant women involved in this study was 73.5% (the pill count method) and this is comparable to the finding reported from south-east Nigeria by Igwegbe *et al.*^[6] However, this rate is higher than figures reported from south-west Nigeria and south Nigeria by Olowookere *et al.*^[10] and Omonaiye *et al.*^[20] respectively, but lower than those reported

Table 3. Sociodemographic characteristics and adherence among HIV-positive pregnant women

Variable	Poor adherence n=45, n (%) [*]	Good adherence n=125, n (%) [*]	p-value
Age group (years)			
<20	5 (1.5)	6 (54.5)	0.214
20 – 35	29 (23.4)	95 (76.6)	
>35	11 (31.4)	24 (68.6)	
Parity			
0	5 (26.3)	14 (73.7)	0.026 [†]
1 – 2	35 (32.7)	72 (67.3)	
>2	5 (11.4)	39 (88.6)	
Marital status			
Married	23 (17.8)	106 (82.2)	0.001 [†]
Single	13 (59.1)	9 (40.9)	
Widowed	5 (50.0)	5 (50.0)	
Divorced	4 (44.4)	5 (55.6)	
Education (women)			
None	17 (40.5)	25 (58.5)	0.005 [†]
Primary	14 (35.0)	26 (65.0)	
Secondary	9 (23.7)	29 (76.3)	
Tertiary	5 (10.0)	45 (90.0)	
Occupation (women)			
Unemployed	13 (44.8)	16 (55.2)	0.001 [†]
Self-employed	9 (28.1)	23 (71.9)	
Privately employed	15 (48.4)	16 (51.6)	
Government employed	8 (10.3)	70 (89.7)	
Religion			
Christianity	23 (21.5)	84 (78.5)	0.055
Islam	22 (34.9)	41 (65.1)	
Place of residence			
Rural	26 (46.4)	30 (53.6)	0.001 [†]
Urban	19 (16.7)	95 (83.3)	
Social class			
Low	28 (29.5)	67 (70.5)	0.602
Middle	10 (23.3)	33 (76.7)	
High	7 (21.9)	25 (78.1)	
Age (years), mean (SD)	30.42 (5.95)	29.74 (5.86)	0.508
Parity, mean (SD)	1.58 (0.89)	1.84 (1.07)	0.144
Gestational age (weeks), mean (SD)	28.27 (3.90)	29.38 (4.12)	0.118
Duration of ART use (years), mean (SD)	3.10 (1.62)	3.38 (1.54)	0.310
CD4 counts (cells/mm ³), mean (SD)	344.47 (84.73)	410.18 (61.19)	0.001 [†]

SD = standard deviation, ART = antiretroviral therapy.

^{*}Unless otherwise indicated – %s of each subcategory.[†]Statistically significant.

from Ethiopia by Shibabaw *et al.*^[15] and Zambia by Ng'ambi *et al.*^[21] The variation in the prevalence rate reported from these studies might be due to differences in the population of the respondents, as well as awareness and practice of PMTCT in the study areas, which were similarly expressed by Ekama *et al.*^[13] and Ng'ambi *et al.*^[21]

Education and occupation of women, partner disclosure of HIV status, having treatment support and use of ARV drugs for PMTCT were the determinants of good medication adherence in this study. A higher level of education was found to be associated with increased likelihood of good medication adherence. Women with at least post-primary education were three times more likely to adhere to their medication regimen than those with no formal education. This finding is consistent with reports from previous studies done in Kano (northern Nigeria), Ethiopia and India.^[12,15,22] In these studies, women with low educational status had poor medication adherence

and the authors emphasised the role of education in reproductive health. Education facilitates communication with health workers, engagement in beneficial health practices and use of maternal health services, including understanding of adherence counselling that would enhance optimal intake of ARV drugs.^[23] Employed women in this study had a higher rate of good adherence to ART. This is in agreement with findings of Shibabaw *et al.*^[15] where women with low monthly income were less adherent to their ARV drug regimen. Being employed financially empowers women and this assists them in taking critical decisions that will improve their health outcomes.^[24]

Serostatus disclosure is an important factor in curtailing HIV spread, including PMTCT, and has been emphasised by the World Health Organization in its HIV counselling and testing protocol.^[25] In this study, women who disclosed their status to their partners showed better adherence. This was similarly reported in previous

Table 4. Clinical characteristics and adherence among the women

Variable	Poor adherence n=45, n (%)*	Good adherence n=125, n (%)*	p-value
Knowledge of HIV			
Poor	38 (58.5)	27 (41.5)	0.001†
Good	7 (6.7)	98 (93.3)	
Partner disclosure			
No	26 (36.6)	45 (63.4)	0.022†
Yes	19 (19.2)	80 (80.8)	
PMTCT			
No	25 (44.6)	31 (55.4)	0.001†
Yes	20 (17.5)	94 (82.4)	
Previous PMTCT			
No	30 (32.6)	62 (67.4)	0.049†
Yes	15 (19.2)	63 (80.8)	
Stigmatisation			
No	10 (11.2)	79 (88.8)	0.001†
Yes	35 (43.2)	46 (56.8)	
Treatment support			
No	29 (40.8)	42 (59.2)	0.001†
Yes	16 (16.2)	83 (83.8)	
ART duration (years)			
<3	17 (30.9)	38 (69.1)	0.234
≥3	28 (24.3)	87 (75.7)	

PMTCT = Prevention of mother-to-child transmission; ART = antiretroviral therapy.
 *Percentages of each subcategory.
 †Statistically significant.

Table 5. Logistic regression analysis of factors associated with medication adherence among HIV-positive pregnant women

Variable	aOR (95% Confidence interval)	p-value
Marital status		
Married	1.25 (0.76 - 2.23)	0.350
Not married	1	
Education		
No formal education	1	
Primary	1.32 (0.95 - 1.98)	0.071
Post-primary	3.03 (1.23 - 5.79)	0.043*
Occupation		
Unemployed	1	
Employed	4.13 (1.83 - 8.15)	0.020*
Partner disclosure		
No	1	
Yes	2.53 (0.99 - 5.80)	0.035*
Previous PMTCT		
No	1	
Yes	2.17 (1.11 - 3.03)	0.220
Treatment support		
No	1	
Yes	2.15 (0.77 - 4.15)	0.014*
PMTCT		
No	1	
Yes	3.15 (0.93 - 6.21)	0.035*
Stigmatisation		
No	1	
Yes	0.78 (0.23 - 2.45)	0.430

PMTCT = prevention of mother-to-child transmission; aOR = adjusted odds ratio.
 *Statistically significant.

studies.^[6,13,26] This is because status disclosure increases social and psychological support for the infected partners, especially from their

spouses. This is further supported by another finding of this study that revealed that women who had treatment support from their relatives including their spouses had almost three times higher odds of adherence to their ARV drug regimen compared with women without support. Previous studies have shown that disclosure of status to partners, family and friends not only guaranteed their support but also resulted in their serving as treatment partners by encouraging them, and this was associated with good maternal adherence and improved clinical outcome.^[6,13,19] HIV-positive women should be counselled and encouraged to disclose their status, although this should be voluntary because of the risk of intimate partner violence.^[13]

The use of ARV drugs for PMTCT of HIV infection was a significant determinant of good adherence in this study. It is therefore not surprising that all the women who had good adherence gave this reason as one of their motivating factors, and they had three times higher odds of adherence than the others. It is probable that these women heard and understood during their adherence counselling that ART during pregnancy is not solely for treating maternal disease but also to prevent infection of their unborn babies. The need for continual adherence counselling in this regard cannot be emphasised enough^[6] because some of the women with poor adherence in this study missed taking their drugs because they felt better.

Marital status, previous PMTCT experience and HIV stigmatisation were not significantly associated with good adherence on logistic regression analysis. The role of marital status in adherence has been inconsistent, with some previous studies revealing a significant association and others not.^[27,28] Previous PMTCT experience was not an independent determinant of good adherence; this was in contrast to reports from Omonaiye *et al.*^[20] and Murithi *et al.*^[29] Both studies found that women who had previously accessed PMTCT successfully (had children who were HIV-negative) were

better prepared and more adherent to their ARV drug regimen in the current pregnancy.^[20,29] Although not significantly associated with adherence, stigmatisation and discrimination remain important factors for non-adherence to ARV drugs because more than half of the women missed their drugs as a result of this. Ekama *et al.*^[13] opined that continual campaigning against stigmatisation and discrimination should be sustained to achieve improved uptake of HIV services and optimal medication adherence.

Women with good adherence in this study reported that their previous PMTCT exposure, living healthily and the desire to protect their unborn baby motivated them to use their ARV drugs. These were also reported in previous studies.^[13] Forgetfulness, busy work schedule, feeling better, side-effects of the drugs and stigmatisation were some of the reasons given by the women who had poor adherence. Similar reasons for non-adherence have also been reported in previous studies.^[10,13,15,30]

Strengths of this study included the fact that it was a multicentre study done in primary and tertiary healthcare centres, and two methods were used in the assessment of adherence among the women, thereby increasing the reliability of the findings. The women's CD4 counts and viral loads, which are used to monitor the progress of the disease, were also measured to correlate their level of adherence. However, the study might be limited by recall bias on the part of the women and the non-use of ARV blood measurement to determine the actual plasma concentration of the ARVs.

Conclusions

This study revealed good adherence in the majority of the HIV-positive pregnant women. A small proportion of them had poor adherence owing to busy work schedule, forgetfulness, feeling better and fear of stigmatisation. Higher education level, being employed, status disclosure, treatment support and the use of ARV drugs for PMTCT were significant determinants of good adherence. Continual counselling on adherence and partner disclosure should be ensured and sustained for all pregnant women on ARVs for maximum benefit and elimination of the risks of MTCT. A longitudinal study will be desirable in future research to follow up babies that are born to these women to evaluate the effectiveness of adherence on PMTCT of HIV.

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